Applied Psychophysiology and Biofeedback, Vol. 31, No. 3, September 2006 (© 2006)
DOI: 10.1007/s10484-006-9018-2

Thermal Biofeedback for Primary Raynaud's Phenomenon: A Review of the Literature

Maria Katsamanis Karavidas,[1,5] Pei-Shan Tsai,[2] Carolyn Yucha,[3] Angele McGrady,[4] and Paul M. Lehrer[1]

Published online: 3 October 2006

The clinical presentation of primary Raynaud's phenomenon (RP) derives from various pathogenic triggers. The use of thermal biofeedback (TBF) may be of benefit in reducing the severity and frequency of attacks. This article summarizes the relevant research regarding the pathophysiology of primary RP and mechanism of TBF for RP. Systematic reviews of the efficacy of TBF for RP and treatment guidelines for clinicians are provided. The panel concludes that the level of evidence for TBF efficacy is categorized as Level IV: efficacious. The rationale, based on three randomized controlled trials conducted in independent laboratories, demonstrated "superiority or equivalence" of treatments that include TBF. However, randomly controlled trials (RCT) with positive clinical outcomes tended to be small. A large RCT with negative results did not effectively teach handwarming skills. Procedures for reviewing and rating of the levels of evidence of efficacy of studies was based on the Template for Developing Guidelines for the Evaluation of the Clinical Efficacy of Psychophysiological Interventions developed by the joint task force of the AAPB and the Society for Neuronal Regulation (SNR).

KEY WORDS: Thermal biofeedback; Primary Raynaud's phenomenon.

INTRODUCTION

Primary Raynaud's Phenomenon

Raynaud's phenomenon (RP) refers to recurrent, episodic vasoconstriction of the digital arteries and arterioles (Block & Sequeira, 2001; Wigley, 2002). The ischemic phase of RP presents clinically as demarcated pale (blanching) or cyanotic skin, limited to the digits (Wigley, 2002). It typically starts in one or several digits after exposure to cold or

[1]University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, Piscataway, New Jersey.
[2]Taipei Medical University, Taipei, Taiwan.
[3]University of Nevada, Las Vegas, NV.
[4]Medical College of Ohio, Toledo, OH.
[5]Address all correspondence to Maria Katsamanis Karavidas, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, Piscataway, New Jersey; e-mail: karavima@umdnj.edu.

stress and may spread symmetrically to both hands. The attack usually ends with a rapid reperfusion of the digits, manifested by erythematous skin (reactive hyperemia).

RP is classified as primary if there is no known cause, and secondary if an associated disorder has been detected (Block & Sequeira, 2001). In practice, clinical criteria are used for distinguishing patients with primary RP from those with secondary RP. The suggested criteria for primary RP include: vasospastic attacks precipitated by cold or emotional stress, the absence of a secondary cause, symmetric attacks, the absence of tissue necrosis, ulceration, or gangrene; a negative test for antinuclear antibody; a normal erythrocyte sedimentation rate; and normal nail fold capillaries (Allen & Brown, 1932; LeRoy & Medsger, 1992). Secondary RP is associated with: onset after age 30 or 40 years; episodes that are intensive, painful, asymmetric, or associated with ischemic skin lesions; connective-tissue disease; specific auto antibodies associated with underlying inflammatory disease; and evidence of microvascular disease on microscopy of nail fold capillaries (Block & Sequeira, 2001; Wigley, 2002). In addition to these clinical criteria, digital blood pressure response to cooling has been used to assess the severity of RP (Jennings et al., 1999; Maricq et al., 2000; Maricq, Valter, & Maricq, 1998). Freedman et al. (1988) used the criteria of Allen and Brown (1932), while other studies, reviewed in this paper, diagnosed RP using a structured interview assisted by color charts. In addition, inclusion criterion is at least two attacks on an average day during the previous cold season. There are no universally accepted medical treatments for primary RP. Initial management usually includes the avoidance of cold temperatures and emotional stress. Calcium-channel blockers are first-line drug therapy (Coffman, 1991) for Raynaud's phenomenon.

Prevalence rates of Raynaud's phenomenon differ by gender (Gardner-Medwin, Macdonald, Taylor, Riley, & Powell, 2001). A questionnaire study conducted in the United States estimated a prevalence of 4.3% in women and 2.7% in men (Weinrich, Maricq, Keil, McGregor, & Diat, 1990), while in the United Kingdom estimated rates were found to range from 19% in women to 11% in men (Simlan, Holligan, Brennan, & Maddison, 1990). These data do not imply, however, that gender differences necessarily result in different symptoms or outcomes in treatment studies. Genders may differ in susceptibility, but respond similarly to treatment where the disorder does occur (Robinson, Gagnon, Riley, & Price, 2003).

Current research suggests that a local abnormality at the digital microcirculation level may be an underlying mechanism (Turton, Kent, & Kester, 1998). An overactivity of the sympathetic nervous system (SNS) is less likely to be the primary abnormality of RP, although early evidence supports the involvement of the SNS-mediated vascular tone in the pathogenesis of the disease (Turton et al., 1998). Research on the pathophysiology of Raynaud's disease indicates that attacks are most probably caused by a hypersensitivity of peripheral vascular $\alpha 2$-adrenergic receptors to cooling (Freedman, Moten, Migaly, & Mayes, 1993). Additionally, peripheral vascular $\alpha 1$-adrenoceptors are hypersensitive in Raynaud's disease patients at baseline (Edwards, Phinney, Taylor, Keenan, & Porter, 1987; Graafsma et al., 1991). Since vascular $\alpha 1$- and $\alpha 2$- adrenoceptors are hypersensitive in Raynaud's disease patients, normal catecholamine elevations that are produced by emotional stress or by reflex cooling can also trigger the vasospastic attacks (Freedman et al., 1993).

Jobe, Sampson, Roberts, and Kelly (1986) found that those with Raynaud's disease were no more emotionally unstable than a normal population. Anxiety scores, as measured by the Institute for Personality and Ability Testing (IPAT) Anxiety Scale Questionnaire (Cattell, 1957) did not differentiate Raynaud's subjects (mean score of 24.1) from the

healthy subjects (mean score of 27.1). Furthermore, the "neuroticism" scores of the Eysenck Personality Questionnaire did not differentiate Raynaud's subjects (mean score of 7.13) from normal subjects (mean score of 8.51).

Similarly, Freedman and Ianni (1983) randomly provided concurrent cognitive stress management training to half of subjects in each of four treatment groups in the study (because emotional stress has been implicated as a trigger for Raynaud's attacks). The addition of cognitive stress management did not significantly affect efficacy.

Behavioral treatment of RP has focused mainly on vasodilatation with or without biofeedback (BF). Feedback-assisted vasodilatation refers to thermal biofeedback (TBF) which teaches the skill of self-regulation of skin temperature (Schwartz & Sedlacek, 2003, pp. 369–381). TBF therapy has been found to reduce both the frequency and severity of vasospastic attacks (Taub & Stroebel, 1978; Sedlacek & Taub, 1996). The goal of TBF therapy is to train subjects to control peripheral vasoconstrictor responses and to acquire voluntary hand warming skills. It is hypothesized that, once learned, hand warming can be produced without feedback. Ideally, trained individuals generate hand warming quickly upon cold exposure, or better yet, prior to cold exposure, to prevent vasospasm. For example, individuals are taught to vasodilate just prior to going outside in cold weather. Once vasospasm has actually occurred, it is difficult to reverse with handwarming. A non-neural beta-adrenergic mechanism as well as a reduction in alpha sympathetic nerve activity may be involved in the vasodilatation produced by TBF (Freedman, Keegan, Migaly, Galloway, & Mayes, 1991; Freedman et al., 1988). Other nonpharmacological therapies designed to reduce emotional stress may also be helpful in preventing Raynaud's attacks.

AIMS

The aims of this review were: (1) to comprehensively examine the level of evidence for efficacy of biofeedback treatment of RP in the published empirical literature; (2) to rate treatment efficacy according to standard guidelines; and (3) to make recommendations based on the findings.

REVIEW METHODOLOGY

MedLine and PsychInfo databases were searched for research articles published in English between 1975 and 2005. The condition of interest (COI) for this review was primary Raynaud's phenomenon. Three search terms were used to identify potential studies. These terms were "Raynaud's," "temperature," and "biofeedback." Studies were restricted to those involving individuals diagnosed with primary RP and those specifically addressing the treatment effect of TBF. We only reviewed papers describing randomized controlled trials (RCT), nonrandomized controlled clinical trials (CCT), and follow-up (FU) studies. Studies that did not include measurements of at least one of the following treatment outcomes were excluded: symptom frequency, symptom intensity, and temperature response to cold.

In this report, the results are synthesized in a narrative format. A meta-analysis was not conducted because few of the trials included the same comparisons and outcomes. A total of ten studies (reported in 12 papers) were included. Efficacy of TBF for the COI refers to "the determination of treatment effect derived from a systematic evaluation obtained in a controlled clinical trial." Rating of the levels of evidence of efficacy was based on

the Template for Developing Guidelines for the Evaluation of the Clinical Efficacy of Psychophysiological Interventions developed by the joint task force of the AAPB and the Society for Neuronal Regulation (SNR) (La Vaque et al., 2002). Five levels of evidence were defined: Level 1—Not empirically supported; Level 2—Possibly efficacious; Level 3—Probably efficacious; Level 4—Efficacious; and Level 5—Efficacious and specific. All papers were evaluated by two independent reviewers who extracted data on study design, sample size, treatment conditions, dosage, outcomes, and quality. If a disagreement occurred in the scoring, a third rater was asked to categorize the study. This was required for only one study; the third reviewer agreed with one of the original reviewers and the rating was resolved.

REVIEW OF BF TRIALS FOR RAYNAUD'S PHENOMENON

A total of ten studies of Raynaud's phenomenon met inclusion criteria for review. Seven were RCT's (see Table IA), one a CCT (see Table IB), and two were FU studies (see Table IC). Of the eight studies reviewed, seven were RCT's. These studies all included predominantly female participants. With the exception of one RCT ($N = 313$), these studies used a small sample size ($N = 12$–39). One study did not report the age of the study participants. A paper by Keefe, Surwit, and Pilon (1979) described follow-up data from a previous study. Surwit, Pilon, and Fenton (1978) and three papers presented various aspects of a single study of the Raynaud's Treatment Study (RTS; Middaugh et al., 2001; Raynaud's Treatment Study Investigators, 2000; Thompson et al., 1999). A critical examination of the reviewed studies highlighted three major shortcomings shared by the majority of the published studies: (1) methodological flaws (e.g., outdoor temperature considered as a confounding variable, ineffective training methods for temperature biofeedback, the absence of TBF alone vs. control group). For example, in a study by Guglielmi, Roberts, and Patterson (1982), the attack rates of TBF, EMG, and no-treatment control groups all dramatically declined (93, 99, and 88%, respectively) as the outdoor temperature became warmer. Three out of ten studies did not account for the seasonal effects element; (2) all-female sample versus a mixed sample, and (3) inconsistencies as a result of gaps in reporting complete demographic data and accurate subject information at baseline.

ADEQUACY OF THERMAL BIOFEEDBACK TRAINABILITY

The failure to detect a *superior beneficial effect* of TBF compared to other general relaxation techniques on Raynaud's symptomatology in some studies may be due to ineffective TBF training. Subjects in some studies did not acquire the skill of voluntary vasodilation when exposed to cold stress. Guglielmi et al. (1982) reported that less than 50% of TBF subjects in their study learned to produce finger temperature increases during training. Similarly, Middaugh et al. (2001) reported that only 35% of TBF subjects met the study criteria for increasing finger temperature. Keefe, Surwit, and Pilon (1980), trained subjects in small groups that met for 3 one-hour sessions. Although subjects in Keefe et al.'s (1979) study achieved digital temperature responses after four weeks of training, results did not persist at a 9-month follow-up.

Other studies document the effectiveness of training to produce a 2–4°F increase in hand warming. Freedman and Ianni (1983) demonstrated that temperature biofeedback

Table I. Summary of Studies Evaluating the Efficacy of TBF for Raynaud's Phenomena

Author(s) (year)	Controlled for seasonal effects	*N*; % Female; age range or mean	Treatment conditions; Training format; Training site	Dosage (hours) × duration (weeks); FU (months)	Outcomes
(A) Randomized Controlled Trials					
Surwit et al. (1978)	*Yes*	30; 100%; 23–54 years	1. TBF + autogenic training	1.5 × 6	No information regarding the degree of hand warming that subjects were able to achieve
	February–March		2. Autogenic training	1	Trained subjects demonstrated significant pre to post improvement both in ability to maintain digital skin temperature during cold stress challenge and in the number of attacks experienced. Trained subjects demonstrated a *32% decrease in number of attacks compared to a decrease of 10% for the controls* (n.s.)
			3. Waiting-list control		Addition of TBF to autogenic training did not provide additional benefit
			Individual Laboratory or home		
Keefe et al. (1980)	*Yes*	21; 100%; –	1. TBF + autogenic training	1 × 3	No information regarding the degree of hand warming that subjects were able to achieve
	January & February		2. Autogenic training	1	Number of attacks per day dropped in all subjects during training & at 1-month follow-up. All subjects showed significant improvement in ability to maintain skin temperature in response to cold during training
			3. Progressive relaxation		No significant differences between three treatment groups
			Group Laboratory		
Freedman and Ianni (1983)	*Yes*	32; 88%; 20–65	1. TBF	2 × 10	TBF subjects achieved an average of .6°C increase in finger temperature during training. Significant temperature increases (.65°C) occurred during a posttraining voluntary control test in those who received TBF but not in those who received autogenic training or EMG BF; *66.8% reduction in frequency of attacks* at one-year follow-up in the TBF group; TBF under cold stress significantly improved voluntary vasodilation at follow-up & produced a significantly greater (*92.5%*) *reduction in symptom frequency*. One half of the subjects were assigned to receive concurrent cognitive stress management
	December–April		2. TBF under cold stress 3. Autogenic training 4. EMG BF	12	
			Individual Laboratory		

Table I. Continued.

Author(s) (year)	Controlled for seasonal effects	*N*; % Female; age range or mean	Treatment conditions; Training format; Training site	Dosage (hours) × duration (weeks); FU (months)	Outcomes
Freedman et al. (1988)	*Yes*	18; 89%; mean = 42	1. TBF	5 × 5	Compared to the pretreatment month, subjects in the TBF group showed a significant decline in attack rates at Year 1 (81.3%) and Year 2 (80.5%) follow-up. The attack rate of the autogenic group did not change significantly at Year 1 (32.3%) or Year 2 (26.3%)
			2. Autogenic training Individual Laboratory	24	
Jacobson et al. (1979)	*No*	12; 75%; 25–47	1. TBF + relaxation (TBF-RT)	0.33 × 6	Both groups demonstrated finger temperature increases during training. BF-RT subjects showed an average of .5°C increase in finger temperature per trial. RT subjects showed an average of 1.4°C increase in skin temperature per trial. No information regarding the pre to post change in attack rates was available. Both groups demonstrated identical post-training outcomes in self-rated improvement in symptom severity (slightly to markedly improved
			2. Relaxation alone (RT) Individual Laboratory	1 & 24	
Guglielmi et al. (1982)	*No*	39; –; 17–54	1. TBF	1 × 20;	No information regarding the degree of hand warming that subjects were able to achieve
			2. EMG relaxation control	5	Less than 50% of the TBF subjects learned to produce finger temperature increases during training. All three groups reported a decrease in number of attacks. TBF group showed *93% decrease in frequency of attacks* compared to *99%* in the EMG group and *88%* in the no-treatment group. No significant differences were found among the three groups
			3. No-treatment control Individual Laboratory		
Raynaud's Treatment Study Investigators (2000)	*Yes*	313; 75%; mean = 45	1. TBF	2 × 5 or 1 × 10; 12	35% of the TBF subjects met the study criteria for increasing finger temperature (1°F above the last 3 min of baseline, .5 above the last 3 min of baseline and 93–94°F or >94°F). TBF did not reduce attacks compared with control BF. Nifedipine-treated subjects showed 56% fewer attacks than TBF group ($p = 0.08$)

Table I. Continued.

Author(s) (year)	Controlled for seasonal effects	*N*; % Female; age range or mean	Treatment conditions; Training format; Training site	Dosage (hours) × duration (weeks); FU (months)	Outcomes
Thompson et al. (1999) Middaugh et al. (2001)	November–February		2. Control BF (EMG) 3. Nifedipine; Individual Laboratory		
(B) Non-Randomized Controlled Trials					
Jobe et al. (1986)	*Yes*	15; 80%; 14–61	1. TBF + EMG BF + relaxation (TBF-RT)	1 × 8 EMG + 1 × 10 Temperature;	Subjects in the CC group showed an increase of 3.9°C and those in the TBF-RT group showed an increase of 4.1°C from pretest to posttest. No information regarding the pre to post change in attack rates was available. No differences between groups in severity & recovery from attacks. Both groups increased the temperature response to cold. The CC group had less pain during attacks at the end of training & less severe attacks than BF group at 1-year follow-up
	January–March		2. Classical-conditioning (CC) Individual Laboratory	12	
(C) Follow-up Trials					
Keefe et al. (1979)	*Yes*	19; 100%; 23–54 years	Same as above	1.5 × 6;	Mean number of vasospastic attacks per day at follow-up (1.2) were approximately equal to the number of attacks at the end of training (1.3/day). n.s. *There was a 42% reduction in vasospastic attacks from the initial week pre-treatment and a 29% reduction from the first week of treatment to one-year followup*. Training effect of improving digital temperature responses during a cold stress challenge was impaired 9 months after training as compared to 4 weeks after training
				9	
Freedman et al. (1985)	*Yes*	32; 88%; 20–65	Same as above	2 × 10;	Symptom reduction persisted for 3 years post-training for both TBF groups
	November–February			36	

Note. BF: biofeedback; CCT: controlled clinical trial; EMG: electromyography; FU: follow-up; RCT: randomized controlled trial; n.s.: non-significant; TBF: thermal biofeedback.

yielded significant temperature increases (0.65°C) and Jacobson, Manschreck, and Silverberg (1979) showed that combination treatment (TBF and relaxation) and relaxation treatment alone produce increases in skin temperature (i.e., 0.5 and 1.4°C respectively). Classical-conditioning training yielded an increase of 3.9°C temperature while the combination training (TBF, EMG biofeedback and relaxation) showed a 4.1°C increase from pretest to posttest (Jobe et al., 1986).

The various TBF protocols reported in the literature also varied widely in intensity of TBF training. The total hours of TBF training ranged between 2 and 23.5 hours held over a 3- to 20-week period. One study (Keefe et al., 1980) adopted a group-approach to TBF training while others (Freedman & Ianni, 1983, 1988; Jacobson et al., 1979; Guglielmi et al., 1982; Middaugh et al., 2001; RTS Investigators, 2000; Surwit et al., 1978; Thompson et al., 1999) used an individual approach.

Several studies did not report the degree of hand warming that subjects were able to achieve and percentage of subjects who actually learned to produce temperature increases (see Table I). Thus, we do not know whether training to criterion would have impacted the pooled outcome.

COMPARISON GROUPS AND TREATMENT FORMATS

Experimental designs varied widely among the studies we reviewed. Four studies (Guglielmi et al., 1982; Jacobson et al., 1979; Keefe et al., 1980; RTS, 2000) examined the efficacy of TBF alone, and compared TBF effects to other relaxation techniques or calcium-channel blocking agents. Others (Freedman & Ianni, 1983; Freedman, Ianni, & Wenig, 1985; Jobe et al., 1986; Keefe et al., 1979) used a combination of relaxation techniques and TBF. An intent-to-treat analysis approach was adopted by the RTS, but not in the other studies. While intent-to-treat analyses allow assessment of clinical effectiveness in the general population, they are less sensitive to efficacy in a population motivated to learn and practice the technique.

Some studies examined the efficacy of TBF compared to an alternative treatment group (e.g., autogenic training, progressive muscle relaxation, classical conditioning, EMG BF, or a calcium channel blocking agent). Several studies used a no-treatment group. Few studies included a placebo control. In one study, EMG BF was used as the control BF condition. Six of the eight reviewed studies demonstrated that TBF did not provide a better outcome to other types of relaxation techniques, classical conditioning, nonthermal BF (e.g., EMG), or a calcium channel blocking agent but this does not show effectiveness for TBF.

Combining TBF with other treatment approaches make it difficult to assess whether TBF is responsible for the therapeutic benefit. In a study by Freedman and Ianni (1983), TBF training under cold stress produced a significantly greater reduction in symptom frequency than TBF alone, autogenic training, or EMG BF, suggesting that cold "challenge" may be an important element in the TBF protocol. An optimal "dosage"or amount of TBF training RP has not been determined.

Two studies (Guglielmi and the RTS) reported substantial problems in teaching hand warming skills. In neither study were the therapeutic effects significant, compared with a no-treatment control (Guglielmi data) or placebo control (RTS, either frontalis

EMG feedback or medication placebo). Guglielmi's study (1) achieved >88% reduction in attack rates in a no-treatment group as well as in two treatment groups; (2) had poor success in training either EMG decreases or temperature increases; and (3) found that attacks for no-treatment and treatment groups systematically declined across the 5 months of the study from January to June, as environmental temperatures increased, indicating that outdoor temperature effects may have been responsible for improvements in attack rates.

SUPERIORITY OR EQUIVALENCE

Freedman and Ianni (1983) and Freedman et al. (1988) demonstrated that TBF produces greater reductions in symptom frequency than either autogenic training or EMG BF. In contrast, other studies (Surwit et al., 1978; Keefe et al., 1980; Jobe et al., 1986; Jacobson et al., 1979) found that TBF produced the same effects in Raynaud's symptom improvement as various relaxation techniques.

In the RTS, as nifedipine-treated group had better outcomes than one treated with TBF (RTS Study Investigators, 2000). Guglielmi et al. (1982) reported decreases in symptom frequency in all study groups including a no-treatment control group. Together, these studies suggest that TBF does not induce specific treatment effects. It is possible that simply participating in a study produces symptom improvement and that favorable outcomes resulted from subjects' expectations of treatment effects. Thus, the improvement in self-reported symptom severity/frequency might be due to nonspecific effects of the treatment modality such as mood, decreased anxiety, etc.

Other controlled investigations have shown that Raynaud's disease patients treated with TBF resulted in significant reductions in symptom frequency, ranging from 67–92%, and maintained for up to 3 years (Freedman & Ianni, 1983; Freedman et al., 1988). In fact, many consider the two studies by Freedman et al. to be the best in the literature, with a rigorous, well-controlled design, lengthy daily diary measures of attack rates, and outcomes assessed annually for three years with careful attention to seasonal temperatures. There were clear and statistically significant differences in favor of TBF, both in hand warming and in reduction of attack rate. The study by Jobe et al. (1986) uniquely compared a classical conditioning procedure (CC) with a TBF + EMG + relaxation procedure. Both groups achieved substantial hand warming (group averages >3.9°C) and both groups made similar clinical improvements. The impact on attacks was measured by self-rated improvements on a scale from 1 to 5 for 3 different aspects of attacks: attack severity, attack painfulness, and time to recover from attacks (duration). Immediately post training, the CC group seemed more improved than the TFB + EMG + relaxation group (4.0 vs. 3.5, $p < .05$) with regard to pain, but the groups were similar in severity and recovery. At one year, the advantage was still with CC, but again for only one of the three measures, this time for severity (4.83 vs. 3.63, $p < .05$); the groups were now similar on pain and duration. From the raw data that was provided, it is evident that both groups rated themselves as substantially improved, immediately post-training, and at one-year follow-up, although there was some advantage to the CC group-on one of three measures, with the groups equivalent on two of three measures at each time point.

EFFICACY RATINGS OF BF FOR RAYNAUD'S DISORDERS

The following ratings, paraphrased here from the published guidelines, are from the AAPB/SNR efficacy rating guidelines (La Vaque et al., 2002):

Level 1: Supported only by anecdotal reports and/or case studies in non-peer reviewed venues. Not empirically supported.

Level 2: *Possibly Efficacious*: At least one study of sufficient statistical power with well identified outcome measures, but lacking randomized assignment to a control condition internal to the study.

Level 3: *Probably Efficacious*: Multiple observational studies, clinical studies, wait list controlled studies, and within subject and intra-subject replication studies that demonstrate efficacy.

Level 4: *Efficacious*: A treatment for a particular condition of interest can only be rated as "efficacious," in the hierarchical rating system for evidence for treatment efficacy, when the following six criteria are met:

1. The experimental treatment has been found in randomized studies to be statistically significant or equal to a control group (no treatment, alternative treatment or placebo group);
2. The studies have been conducted on well-defined subjects with a specific problem for whom inclusion criteria are delineated in a reliable, operationally defined manner, and
3. The studies used valid and clearly specified outcome measures related to the problem being treated and,
4. The data are appropriately analyzed;
5. Diagnostic and treatment procedures are clearly defined in a manner that makes replication by others possible; and
6. The superiority or equivalence of the investigational treatment has been shown in at least two independent research settings.
   Evidence of *Level 5*: Efficacious and Specific (the investigational treatment has been shown to be statistically superior to credible sham therapy, pill, or alternative bona fide treatment in at least two independent research settings).

The panel concludes that the level of evidence of efficacy for TBF is categorized as Level IV: efficacious. There are RCT's from three independent labs: Surwit et al. (1978), Keefe et al. (1980) and Freedman et al. (1988) demonstrating "superiority or equivalence" of treatments that include TBF. Certainly the criteria for Level III: Probably Efficacious are met; the Freedman RCTs demonstrate specific effects plus four other RCTs demonstrate efficacy. Level V: efficacious and specific, is not as yet reached because there is evidence of specific effects in one research setting but not two. Thus, the case for specific effects has not yet been made. As a caveat, however, all three RCT's with positive results were small studies. The one large RCT, the RCT trial, had negative results but did not achieve significant hand warming effects, so the adequacy of the training technique in that study is in doubt.

TREATMENT GUIDELINES

TBF is widely used by clinicians to treat RP. A typical TBF research study training session includes a 10–15-min waiting or adaptation period, a 10–15-min baseline period, a 15–20-min TBF training period, and a 10–20-min verbal review of the session. The typical number of sessions of treatment reported in the studies reviewed is between 5 and 10, although some individuals may require 8 to16 sessions or even more to learn hand-warming skills. Hand-warming skills are difficult to learn, but the acquisition of these skills is essential to favorable treatment outcomes. In most RCT's, a predetermined set of sessions was administered to all participants to ensure the consistency of the training protocol. In practice, however, patients are usually trained to a criterion level of mastery rather than a set number of sessions to ensure the acquisition of the specific vasodilation response. We recommend that future TBF training protocols include testing transfer of training and generalization of vasodilation (or reduced vasoconstriction) response from the laboratory to real-life situations. One or two TBF sessions should be conducted under cold stress conditions. A no-feedback session during which subjects are to increase finger temperature without feedback may also be useful. Home practice with or without feedback devices is encouraged.

Optimally, the goal of any treatment modality for Raynaud's disease is to reduce the vasoconstriction response to cold and other stressors. To ensure an optimal beneficial outcome, a multiple treatment approach is recommended over a single modality approach, in order to maximize the chances of a favorable response. Some types of relaxation techniques such as progressive muscle relaxation, frontalis EMG BF, or autogenic training can be introduced before the actual TBF training. Guided imagery that is tailored to the individual subject to increase relaxation and warming can also be incorporated into treatment plans.

CONCLUSIONS

Procedures for training subjects in TBF varied across studies, both in length of training, training environment and instructor contact. In fact, many of the studies did not outline the qualifications and training received by their own biofeedback technicians. It is possible that the trainer characteristics rather than the intervention explained the varying "trainability." For example, Taub and School (1978) showed that an overly impersonal approach to TBF training interferes with learning to warm the hands. This may explain the poor results of two major studies (Guglielmi and RTS) that documented limited success in training subjects with TBF. Guglielmi et al. (1982) indicated that, while the lab technician offered support and encouragement to the subjects on their performance, the experimenter in the adjacent room was given explicit instructions to limit his/her interactions to a simple greeting when subject arrived for their weekly sessions. Subjects were offered "support and encouragement" during training, but it is not clear the extent and detail of performance feedback offered by lab technicians, or the interpersonal warmth between therapist and patient. Both groups were asked to refrain from seeking additional information on the topic of biofeedback. One can surmise that the research assistants themselves could therefore provide only limited feedback to subjects since they themselves were restricted by the research procedures. Limited feedback and an overly controlled environment could also

have lead to a sterile learning environment. In the RTS study, where verbal coaching was only provided *after* the biofeedback phase to the cohort 1 group (November–February 1993 and 1994) coaching resulted in a 32% increase in finger temperature. Since learning was less than expected, participants in cohort 2 (November–February 1994–1995) were coached *during* the feedback phase. The modification in feedback resulted in an additional 4% increase in finger temperature (*n.s.*). Overall, only 35% of the Raynaud's subjects and 67% healthy individuals achieved study standards for "successful learning" ($p < .001$).

Perhaps excessive digital vasoconstriction, due to Raynaud's disease, may override TBF vasodilation. Yet, multiple studies have shown that hand warming can be easily learned in this population. Middaugh et al. (2001) found that gender, coping skills and anxiety were significant predicators of trainability. It is more likely that the Raynaud's population is hypersensitive to sensations in their periphery and thus may harbor additional fears about interventions further increasing pain. Failed interventions and lack of consensus from the medical community of the pathology and role of anxiety are just some factors that can contribute in making Raynaud's patients less optimistic and open to the effectiveness of TBF. Interpersonal warmth may be particularly important in allowing an anxious patient to relax and is a key element in biofeedback training.

FUTURE DIRECTIONS

This paper systematically reviewed eight controlled clinical trials and two follow-up studies that examined the efficacy of TBF for primary RP. The level of evidence of efficacy for TBF was rated as Level IV: efficacious based on the AAPB/SNR criteria. Several study limitations were noted in the studies reviewed. The panel recommends that future research on TBF for RP should meet the following conditions:

1. Better specification of duration of the disease, since onset, gender and age of participants, and medication status;
2. More consistent criteria for study outcomes;
3. Better specification of dosage, duration, and format of the TBF protocol;
4. Inclusion of strategies to control for placebo and/or nonspecific effects; and
5. Continued use of placebo and no treatment controls
6. Inclusion of learning criteria for TBF training.
7. Evaluation of maximally effective forms of treatment, including a personally warm interaction with the therapist, with treatment elements and pacing of treatment closely reflecting that used in clinical practice.

For clinical practice, treatment guidelines for use of TBF for primary RPT are as follows:

1. Subjects should be trained to a predetermined criteria (i.e., voluntarily raising temperature to 93°F for at least 15 min [Sedlacek, 1979]) to ensure the acquisition of the specific vasodilation response.
2. Include cold stress conditions in the training.
3. Include a no feedback session to facilitate the transfer of skills outside the laboratory.
4. Include home practice and applied practice in the natural environment.

5. Consider a multiple treatment approach.
6. Address anxiety and comorbid emotional disorders that may complicate treatment.

REFERENCES

Allen, E. V., & Brown, G. E. (1932). Raynaud's disease: a critical review of minimal requisites for diagnosis. *American Journal of Medical Science*, *183,* 187–200.

Block, J. A., & Sequeira, W. (2001). Raynaud's phenomenon. *The Lancet*, *357,* 2042–2048.

Cattell, R. B. (1957). *IPAT anxiety scale*. Institute for Personality and Ability Testing, Champaign, IL.

Coffman, J. D. (1991). Raynaud's phenomenon. *Hypertension*, *17,* 593–602.

Freedman, R. R., & Ianni, P. (1983). Role of cold and emotional stress in Raynaud's disease and scleroderma. *British Medical Journal*, *287,* 1499–1502.

Freedman, R. R., Ianni, P., & Wenig, P. (1985). Behavioral treatment of Raynaud's disease: Long-term follow-up. *Journal of Consulting and Clinical Psychology*, *53,* 136.

Freedman, R. R., Sabharwal, S. G., Ianni, P., Desai, N., Wenig, P., & Mayes, M. (1988). Nonneural beta-adrenergic vasodilating mechanism in temperature biofeedback. *Psychosomatic Medicine*, *50,* 394–401.

Freedman, R. R., Moten, M., Migaly, P., & Mayes, M. (1993). Cold-induced potentiation of a2-adrenergic vasoconstriction in idiopathic Raynaud's disease. *Arthritis and Rheumatism*, *36,* 685–690.

Gardner-Medwin, J. M., Macdonald, I. A., Taylor, J. Y., Riley, P. H., & Powell, R. J. (2001). Seasonal differences in finger skin temperature and microvascular blood flow in healthy men and women are exaggerated in women with primary Raynaud's phenomenon. *British journal of Clinical Pharmacology*, *52,* 17–23.

Graafsma, S. J., Wollersheim, H., Droste, H. T., ten Dam, M. A. G. J., van Tits, L. J. H., Reyenga, J., de Miranda, J. F. R., & Thien, T. (1991). Adrenoreceptors on blood cells from patients with primary Raynaud's phenomenon. *Clinical Science*, *80,* 325–331.

Guglielmi, R. S., Roberts, A. H., & Patterson, R. (1982). Skin temperature biofeedback for Raynaud's disease: A double-blind study. *Biofeedback and Self-Regulation*, *7,* 99–120.

Jacobson, A. M., Manschreck, T. C., & Silverberg, E. (1979). Behavioral treatment for Raynaud's disease: A comparative study with long-term follow-up. *American Journal of Psychiatry*, *136,* 844–846.

Jennings, J. R., Maricq, H. R., Canner, J., Thompson, B., Freedman, R. R., Wise, R., et al. (1999). A thermal vascular test for distinguishing between patients with Raynaud's phenomenon and healthy controls. Raynaud's Treatment Study Investigators. *Health Psychology*, *18,* 421–426.

Jobe, J. B., Sampson, J. B., Roberts, D. E., & Kelly, J. A. (1986). Comparison of behavioral treatment for Raynaud's disease. *Journal of Behavioral Medicine*, *9,* 89–96.

Keefe, F. J., Surwit, R. S., & Pilon, R. N. (1979). A 1-year follow-up of Raynaud's patients treated with behavioral therapy techniques. *Journal of Behavioral Medicine*, *2,* 385–391.

Keefe, F. J., Surwit, R. S., & Pilon, R. N. (1980). Biofeedback, autogenic training, and progressive relaxation in the treatment of Raynaud's disease: A comparative study. *Journal of Applied Behavior Analysis*, *13,* 3–11.

La Vaque, T. J., Corrydon, H., Trudeau, D., Monastra, V., Perry, J., Lehrer, P., et al. (2002). Template for developing guidelines for the evaluation of the clinical efficacy of psychophysiological interventions. *Applied Psychophysiology and Biofeedback*, *27*(4), 273–281.

LeRoy, E. C., & Medsger, T. A. (1992). Raynaud's phenomenon: A proposal for classification. *Clinical and Experimental Rheumatology*, *10,* 485–488.

Maricq, H. R., Jennings, J. R., Valter, I., Frederick, M., Thompson, B., Smith, E. A., et al. (2000). Evaluation of treatment efficacy of Raynaud phenomenon by digital blood pressure response to cooling. Raynaud's Treatment Study Investigators. *Vascular Medicine*, *5,* 135–140.

Maricq, H. R., Valter, I., & Maricq, J. G. (1998). An objective method to estimate the severity of Raynaud phenomenon: Digital blood pressure response to cooling. *Vascular Medicine*, *3,* 109–113.

Middaugh, S. J., Haythornthwaite, J. A., Thompson, B., Hill, R., Brown, K. M., Freedman, R. R., et al. (2001). The Raynaud's treatment study: Biofeedback protocols and acquisition of temperature biofeedback skills. *Applied Psychophysiology and Biofeedback*, *26,* 251–278.

Raynaud's Treatment Study (RTS) Investigators. (2000). Comparison of sustained-release nifedipine and temperature biofeedback for treatment of primary Raynaud phenomenon. *Archives of Internal Medicine*, *160,* 1101–1108.

Robinson, M. E., Gagnon, C. M., Riley, J. L., & Price, D. D. (2003). Altering gender role expectations: effects on pain tolerance, pain threshold, and pain ratings. *Journal of Pain*, *4,* 284–288.

Schwartz, M. S., & Sedlacek, K. (2003). Raynaud's disease: selected issues and considerations in using biofeedback therapies. In M. S. Schwartz, & F. Andrasik (Eds.), *Biofeedback: a practitioner's guide* (3rd ed.). (pp. 369–381). NY: The Guilford Press.

Sedlacek, K. (1979). Biofeedback for Raynaud's disease. *Psychosomatics*, *20,* 535–541.
Sedlacek, K., & Taub, E. (1996). Biofeedback treatment of Raynaud's disease. *Professional Psychology: Research and Practice*, *27,* 548–553.
Simlan, A., Holligan, S., Brennan, P., & Maddison, P. (1990). Prevalence of symptoms of Raynaud's phenomenon in general practice. *British Medical Journal*, *301,* 590–592.
Surwit, R. S., Pilon, R. N., & Fenton, C. H. (1978). Behavioral treatment of Raynaud's disease. *Journal of Behavioral Medicine*, *1,* 323–335.
Taub, E., & School, P. J. (1978). Some methodological considerations in thermal biofeedback training. *Behavior Research Methods and Instrumentation*, *10*(5), 617–622.
Taub, E., & Stroebel, C. F. (1978). Biofeedback in the treatment of vasoconstrictive syndromes. *Biofeedback and Self Regulation*, *3*(4), 363–373.
Thompson, B., Geller, N. L., Hunsberger, S., Frederick, M., Hill, R., Jacob, R. G., et al. (1999). Behavioral and pharmacological interventions: The Raynaud's treatment study. *Controlled Clinical Trials*, *20,* 52–63.
Turton, E. P. L., Kent, P. J., & Kester, R. C. (1998). The etiology of Raynaud's phenomenon. *Cardiovascular Surgery*, *6,* 431–440.
Weinrich, M. C., Maricq, H. R., Keil, J. E., McGregor, A. R., & Diat, F. (1990). Prevalence of Raynaud's phenomenon in the adult population of South Carolina. *Journal of Clinical Epidemiology*, *43,* 1343–1349.
Wigley, F. M. (2002). Raynaud's phenomenon. *New England Journal Medicine*, *347,* 1001